

## Claims

What is claimed is:

- 5 ~~1.~~ A method of expanding a population of cells, the method comprising steps of:  
providing at least one cell with less than wild type p21 activity; and  
expanding the cell population.
- 10 2. The method of claim 1, wherein the step of providing comprises:  
providing a cell; and  
disrupting p21 gene.
- 5 3. The method of claim 1, wherein the step of providing comprises:  
providing a cell; and  
contacting the cell with an agent, wherein the agent inhibits p21 activity.
- 20 ~~4.~~ A method of expanding a population of cells, the method comprising the steps of:  
providing at least one cell with less than wild type p27 activity and less than wild  
type p21 activity; and  
expanding the cell population.
- 25 5. The method of claim 4, wherein the step of providing comprises:  
providing a cell; and  
disrupting p27 and p21 genes.
6. The method of claim 4, wherein the step of providing comprises:  
providing a cell; and  
contacting the cell with an agent, wherein the agent inhibits p27 and p21 activity.
- 30 7. The method of claim 1, wherein the cell is a stem cell.

8. The method of claim 1, wherein the cell is a hematopoietic stem cell.

9. The method of claim 1, wherein the cell is a hematopoietic progenitor cell.

5

10. The method of claim 1, wherein the cell is an erythropoietic cell.

11. The method of claim 1, wherein the cell is a granulopoietic cell.

10 12. The method of claim 1, wherein the cell is a thrombopoietic cell.

13. The method of claim 1, wherein the cell is a neural cell.

14. The method of claim 1, wherein the cell is selected from the group consisting of renal cell, gastrointestinal cell, hepatic cell, skin cell, lung cell, muscle cell, and cardiac muscle cell.

15. The method of claim 1, wherein the cell is an adult-derived stem cell.

16. The method of claim 1, wherein the cell is an embryonically derived stem cell. <sup>SAW<sup>3</sup></sup>

17. The method of claim 1, wherein the cell is a pluripotent stem cell.

18. The method of claim 1, wherein the cell is a multi-potential stem cell.

25 19. The method of claim 1, wherein the cell is a fetal cell. <sup>SAW<sup>2</sup></sup>

20. The method of claim 1, wherein the cell is an embryonic cell. <sup>SAW<sup>2</sup></sup>

21. The method of claim 1, wherein the cell is a mesenchymal cell.

30

22. The method of claim 3, wherein the agent is a protein.

23. The method of claim 3, wherein the agent is a peptide.

5 24. The method of claim 3, wherein the agent is a polynucleotide.

25. The method of claim 3, wherein the agent is a chemical compound.

26. The method of claim 3, wherein the agent is an antibody or fragment thereof.

10

27. The method of claim 3, wherein the agent is an antisense agent.

28. The method of claim 3, wherein the agent is a triple helix forming agent.

15

29. The method of claim 3, wherein the agent is an aptamer.

~~30.~~ A cell with less than wild type p21 activity.

~~31.~~ A cell with at least one copy of the p21 gene disrupted.

20

~~32.~~ A cell with both copies of the p21 gene disrupted.

~~33.~~ A cell with less than wild type p27 activity.

25 ~~34.~~ A cell with at least one copy of the p27 gene disrupted.

~~35.~~ A cell with at least one copy of the p27 gene and p21 gene disrupted.

36. The cell of claim 30, wherein the cell is a stem cell.

30

37. The cell of claim 30, wherein the cell is a progenitor cell.

~~38.~~ A stem cell with increased cyclin activity.

5 ~~39.~~ A progenitor cell with increased cyclin activity.

~~40.~~ A stem cell with increased cyclin-dependent kinase activity.

~~41.~~ A progenitor cell with increased cyclin-dependent kinase activity.

10

42. A pharmaceutical composition comprising a therapeutically effective amount of cells of claim 30.

43. A pharmaceutical composition comprising a therapeutically effective amount of stem cells of claim 36.

44. A pharmaceutical composition comprising a therapeutically effective amount of progenitor cells of claim 37.

45. A pharmaceutical composition comprising a therapeutically effective amount of cells of claim 30, and a pharmaceutically acceptable excipient.

~~46.~~ A non-human transgenic animal wherein at least one copy of the p21 gene is altered.

25 ~~47.~~ A non-human transgenic animal wherein both copies of the p21 gene are altered.

~~48.~~ A non-human transgenic animal wherein at least one copy of the p27 gene is altered in the hematopoietic cell line.

~~49.~~ A non-human transgenic animal wherein both copies of the p27 gene are altered in the hematopoietic cell line.

5 ~~50.~~ A non-human transgenic animal wherein at least one copy of the p27 gene is altered and at least one copy of p21 gene is altered.

~~51.~~ A non-human transgenic animal wherein both copies of p27 gene and both copies of p21 gene are altered.

10 ~~52.~~ The non-human transgenic animal of claim 46 wherein the animal is a mouse.

~~53.~~ The non-human transgenic animal of claim 46 wherein the animal is a rat.

~~54.~~ A transgenic plant with at least one copy of the p21 gene altered.

15 ~~55.~~ A transgenic plant with both copies of the p21 gene altered.

~~56.~~ A method of gene therapy, the method comprising steps of:  
providing at least one cell with less than wild type p21 activity; and  
altering genome of said cell.

~~57.~~ A method of gene therapy, the method comprising the steps of:  
providing at least one cell with less than wild type p27 activity; and  
altering genome of said cell.

25

~~58.~~ A method of gene therapy, the method comprising the steps of:  
providing at least one cell with less than wild type p27 activity and p21 activity;  
altering genome of said cell.

59. The method of claim 56, the method comprising the additional step of delivering the cell to an animal.

60. The method of claim 56, wherein the cell is a stem cell.

5

61. The method of claim 56, wherein the cell is a progenitor cell.

62. The method of claim 56, wherein the cell is a hematopoietic stem cell.

10

63. The method of claim 56, wherein the cell is a hematopoietic progenitor cell.

~~64.~~ A method of gene therapy, the method comprising steps of:  
providing at least one cell with less than wild type p27 activity;  
altering the genome of the cell; and  
transplanting into an individual a therapeutically effective amount of cells  
wherein the percentage of transplanted altered cells is less than 10% of  
total cells transplanted.

5

~~65.~~ A method of gene therapy, the method comprising steps of:  
providing at least one cell with less than wild type p21 activity;  
altering the genome of the cell; and  
transplanting into an individual a therapeutically effective amount of cells  
wherein the percentage of transplanted altered cells is less than 10% of total cells transplanted.

20

25 ~~66.~~ A method of gene therapy, the method comprising steps of:  
providing at least one cell with less than wild type p21 and p27 activity;  
altering the genome of the cell; and  
transplanting into an individual a therapeutically effective amount of cells  
wherein the percentage of transplanted altered cells is less than 10% of total cells transplanted.

30

67. The method of claim 64, wherein the percentage of transplanted altered cells is less than 25% of total cells transplanted.

5 68. The method of claim 64, wherein the percentage of transplanted altered cells is less than 50% of total cells transplanted.

69. The method of claim 64, wherein the percentage of transplanted altered cells is less than 5% of total cells transplanted.

10 70. The method of claim 64, wherein number of cells transplanted is sufficient to allow the altered cells to expand *in vivo* and compete out wild type cells in the individual.

5 71. The method of claim 64, wherein number of cells transplanted is sufficient to allow the altered cells to expand *in vivo* and account for at least 50% of the individual's cells of the transplanted type.

72. The method of claim 64, wherein number of cells transplanted is sufficient to allow altered cells to expand *in vivo* and account for at least 75% of the individual's cells of the transplanted type.

20 73. The method of claim 64, wherein number of cells transplanted is sufficient to allow altered cells to expand *in vivo* and account for at least 90% of the individual's cells of the transplanted type.

25 ~~74.~~ A method of tissue regeneration, the method comprising steps of:  
providing at least one cell with less than wild type p21 activity; and  
administering the cell to an individual in need of tissue regeneration.